BOOK REVIEWS

Genetic Paradigms

The *lac* Operon. A Short History of a Genetic Paradigm. BENNO MüLLER-HILL. De Gruyter, Hawthorne, NY, 1996. x, 207 pp., illus. Paper, $35.95, DM 54, öS 400, or sFr 54. ISBN 3-11-014830-7.

This book was motivated by the inability of a Ph.D. student during an oral exam to tell the author what Max Delbrück did, even though they worked in the eponymous laboratory. Müller-Hill laments, "Molecular Biology has no history for the young scientist." The result is a book that begins with Noah and ends with Goethe. In between is a terse but complete narrative of the genetic vehicle that allowed the working out of the Central Dogma and the regulation of gene expression. Müller-Hill's scientific career spans the entire development of the *lac* operon from theory through repressor isolation, DNA sequencing, and protein three-dimensional structures. It began with his β-galactosidase mechanistic studies as a thesis project and the isolation of Lac repressor as a postdoc with Walter Gilbert. His productive laboratory in Cologne sequenced the repressor protein and has unfolded much of the complexity of *lac* operon regulation in the past two decades. Although Müller-Hill started life as a chemist, this book is the perspective of a geneticist. It is one part chronicle, one part memoir, and one part scientific review. The time is right for this retrospective, since molecular structures of β-galactosidase and the repressor with DNA have just been worked out.

Part 1 begins with the background to the Cartesian publications of François Jacob and Jacques Monod. It ends in 1976, when Monod died and Gilbert, distracted by DNA sequence determination, failed to attend the second Cold Spring Harbor *lac* operon reunion. What most students see in today's biology and genetics textbooks as the paradigm of gene regulation is the picture of 1976.

Part 2, Misinterpretations, is in the spirit of the *au courant* memoir, stopping short of revealing alcoholism or mental illness. In addition to describing several *faux pas* from his own laboratory, the author names names, pointing out, with literature citations, the gaffes of noted geneticists, biochemists, crystallographers, and genome lexicographers, some dead, most living. The list is not all-inclusive but reflects the centrality of the *lac* operon in the epistemology of gene regulation.

Part 3 is an excellent scientific review of the current knowledge of transcriptional regulation in the *lac* operon and its uses as vector and indicator in eukaryotic systems. Today's molecular biology was presaged in the study of the *lac* operon. A genetic vector with overproduction was first constructed for the isolation of Lac repressor (and amber suppressor Su III$^+$ RNA) in order to do biochemistry. Analysis of the *lac* operator DNA by Gilbert led to the sequence of the *lac*I gene by Philip Farabaugh. Combined with the Herculean genetics of Jeffrey H. Miller, this sequence foreshadowed p53 hot spots and malleability of DNA with tandem repeats.

Absent from Müller-Hill's account is the introduction of allostery by Monod, J.-P. Changeux, and Jacob in 1963—an essential feature of macromolecular control through small-molecule interaction. Also missing are the von Hippel school's attempts to understand Lac repressor specificity and thermodynamics in the context of the other 4.7 million base pairs of genomic DNA and the ions of the intracellular milieu.

Müller-Hill declares the *lac* operon a paradigm because of the biological principle that "what works survives; what does not work becomes extinct. Elegant solutions are used again and again. Paradigmatic systems have thus revealed their beauty earlier than others." Actually, there are three practical reasons for the *lac* operon's paradigmatic position: (i) β-galactosidase activity has a 1000-fold dynamic range upon induction; (ii) isopropyl-thio-β-galactoside is a gratuitous inducer, not affected by β-galactosidase; (iii) when hydrolysed by β-galactoside, X-gal gives the familiar blue color to bacterial colonies on plates or to tissues.

Müller-Hill's real lament is not lack of interest in history but a paradigm shift in biological research foreseen by Gilbert in 1991 (*Nature* **349**, 99): to the high school student biological research is now surfing the Internet; to undergraduates it is PCR amplification of c-DNA libraries; to graduate students it is genetics experiments by sequence homology searches through a genome database; and to the rest of us old geezers it is word-processing rearrangement of manuscripts, proposals, and unread photocopied publications. There is still a lot to do. For a structural biologist, the RNA polymerase entry at the *lac* promoter is a vast void. The recent publication by Inada *et al.* (*Genes to Cells* **1**, 293 [1996]) on interplay between glucose and lactose and the *lac* operon will require major textbook revision.

Who should read the present book? All textbook authors and teachers must read parts 1 and 3. Students should read part 2 to see that some giants, including their thesis advisers, have clay feet.

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A Physical Atelier

The Quantum Theory of Fields. Vol. 2, Modern Applications. STEVEN WEINBERG. Cambridge University Press, New York, 1996. xxii, 489 pp., illus. $47.95 or £32.50. ISBN 0-521-55002-5.

Some time ago I visited a harpsichord-maker in his workshop. The artisan showed me his materials, explained the various stages in the construction of harpsichords, then treated me to a recording of Igor Kipnis playing a fandango on one of his instruments. But the object he took the greatest pleasure in showing me was not a finished harpsichord but a block plane—clean, precise, and utterly apt—that he had built in order to sculpt soundboards of surpassing beauty and eloquence. This maker of wonderful instruments was also a maker of wonderful tools.

Reading volume 2 of *The Quantum Theory of Fields* took me back to the harpsichord-maker's workshop, because Steven Weinberg is one of our most gifted makers of theoretical tools as well as a virtuoso in their use. His new book conveys both the satisfaction of understanding nature and the feel of the atelier, for the "modern applications" of its subtitle include both the derivation of physical consequences and the development of new tools for understanding and applying field theory itself.

Quantum field theory is the theory of matter and its interactions that grew out of efforts begun in the late 1920s to join quantum mechanics and relativity. Thanks in considerable measure to its successes over the past quarter-century, quantum field theory has become the preferred conceptual

and mathematical framework for approaching many of the fundamental problems of physics. Indeed, it is the resemblance among the field theories of the strong, weak, and electromagnetic interactions that inspires the hope for a unified theory of them all.

Two great themes are at the heart of "Modern Applications": the role of symmetry in determining the fundamental interactions and the concept of symmetries that are hidden at low energies. Weinberg's treatment of non-Abelian gauge theories—specifically quantum chromodynamics, the theory of strong interactions among quarks—is notable for an explicit calculation of the quantum corrections that make the coupling constant of the theory depend on the energy scale. This illuminates the remarkable feature of "asymptotic freedom," whereby the strong interactions become feeble—and susceptible to analysis by perturbation theory—at high energies. This leads in turn to a clear and thorough presentation of the varieties of asymptotic behavior for a field theory, using the methods of the renormalization group.

Hidden symmetries are treated in two masterly chapters devoted to global and local symmetries. The discussion of the pion as an avatar of chiral symmetry-breaking integrates the fruitful current-algebra approach of the 1960s with our modern understanding based on quantum chromodynamics. A highlight of the chapter on local symmetries is a rich discussion of superconductivity as a consequence of the spontaneous breaking of electromagnetic gauge symmetry. The superconducting phase transition is our model for hiding the electroweak symmetry, and a detailed examination using the tools of modern field theory is rewarding.

As quantum field theory and gauge theories have become more central to our study of physics at very short distances, or very high energies, we have changed our attitude about the theories themselves. We no longer demand that our theories make sense up to arbitrarily high energies but regard them as effective theories that are appropriate to describe the important physics in various energy regimes. In many instances, effective field theories provide the most convenient tool for working out the consequences of symmetries and the general principles underlying quantum field theory. Among the many tools Weinberg presents, he shows effective field theories with particular pleasure.

The Quantum Theory of Fields: Modern Applications is a splendid book, with abundant useful references to the original literature. It is a very interesting read from cover to cover, for the wholeness Weinberg's personal perspective gives to quantum field theory and particle physics. An author index and a well-chosen subject index make "Modern Applications" a valuable reference book.

For a highly motivated and superbly prepared student, *The Quantum Theory of Fields: Modern Applications* could serve as a textbook, with or without its companion volume "Foundations." The ideas of each chapter are elaborated by several thought-provoking problems. I will recommend it to students who have completed a first course in field theory and hope that many of my colleagues will read it as well. Weinberg leads us to a frontier rich in possibilities. This is an optimistic book, written with much respect for ideas and nature—and for tools.

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NO Methodology

Nitric Oxide Synthase. Characterization and Functional Analysis. MAHIN D. MAINES, Ed. Academic Press, San Diego, 1996. xviii, 354 pp., illus. $89 or £65. ISBN 0-12-185301-2. Methods in Neurosciences, vol. 31.

Shortly after the discovery that nitric oxide is the principal form of the endothelium-derived relaxing factor, it was shown to modulate synaptic plasticity during learning and development, to regulate cerebral blood flow, and to have a pathological role in neuronal degeneration. Although the biological lifetime of nitric oxide is probably less than a second, its half-life is long relative to the time scales involved in neural transmission, allowing it to diffuse between neurons and act as a retrograde messenger to locally modulate neuronal activity. The importance of nitric oxide for the functioning of the central nervous system is underscored by the fact that the brain contains more nitric oxide synthase than any other tissues in the body under non-pathological conditions. Furthermore, the neuronal nitric oxide synthase gene may have the most complex organization of any gene expressed in the central nervous system (see P. A. Marsden, *Adv. Pharmacol.* **34**, 71–90 [1995]), undergoing complex regulation during development and after CNS injury.

Nitric Oxide Synthase: Characterization and Functional Analysis is a timely discussion for neuroscientists of practical methods for studying nitric oxide. The contributions are organized into three sections dealing with the detection of nitric oxide, the expression, purification, and gene regulation of nitric oxide synthases, and the assessment of nitric oxide–mediated functions at the cell and organ levels. Most of the chapters are authored by pioneering investigators and provide an amount of detail appropriate to initiate newcomers to the field.

In the past few months, three new volumes—volumes 268 and 269 of *Methods in Enzymology* edited by L. Packer (Academic Press) and *Methods in Nitric Oxide Research* edited by M. Feelisch and J. Stamler (Wiley)—have addressed more general methodological approaches. Each has its strengths. For example, the *Methods in Enzymology* volumes cover the peroxynitrite– and nitric oxide–derived oxidants in greater detail, and the Feelisch and Stamler book contains excellent discussions of nitric oxide donors and the chemistry of nitric oxide. Because of the youth and breadth of nitric oxide research, it is best for investigators to consult and compare all four volumes.

Like any new field nitric oxide research still has many potential artifacts and pitfalls, which are only partially addressed in any of the four books now available. For example, one matter concerning which understanding needs to be more fully developed is the differences between nitric oxide donors and nitric oxide. The donors are often more reactive than nitric oxide itself, and considerable caution should be exercised before concluding that their actions applied to tissues in millimolar concentrations mimic the physiological production of nitric oxide itself.

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Books Received

Advanced Catalysts and Nanostructured Materials. Modern Synthetic Methods. William R. Moser, Ed. Academic Press, San Diego, 1996. xxvi, 592 pp., illus. $85. ISBN 0-12-508460-9.

Bohmian Mechanics and Quantum Theory. An Appraisal. James T. Cushing, Arthur Fine, and Sheldon Goldstein, Eds. Kluwer, Norwell, MA, 1996. viii, 403 pp., illus. $159 or £108 or Dfl. 245. ISBN 0-7923-4028-0. Boston Studies in the Philosophy of Science, vol. 184. From a conference, Bielefeld, Germany, July 1995.

Concepts in Vaccine Development. Stefan H. E. Kaufmann, Ed. De Gruyter, Hawthorne, NY, 1996. xxii, 583 pp., illus. $119 or DM 178 or öS 1.317 or sFr 171. ISBN 3-11-014815-3.

Developmental Science. Robert B. Cairns, Glen H. Elder, Jr., and E. Jane Costello, Eds. Cambridge University Press, New York, 1996. xx, 291 pp., illus. $44.95. ISBN 0-521-49585-7. Cambridge Studies in Social and Emotional Development.

Electronic Noise and Fluctuations in Solids. Sh. Kogan. Cambridge University Press, New York, 1996. xviii, 354 pp., illus. $84.95. ISBN 0-521-46034-4.